PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:

Applicant	:	Gopi M. Venkatesh et al.
Serial No.	:	10/713,929
Filed	:	November 14, 2003
Title	:	MODIFIED RELEASE DOSAGE FORMS OF SKELETAL MUSCLE RELAXANTS
Docket	:	451194-101
Examiner	:	David L. Vanik
Art Unit	:	1615

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Sir:

PRE-APPEAL BRIEF REQUEST FOR REVIEW

This request is filed in response to the final Office action dated June 13, 2007 and is accompanied by a Notice of Appeal and the applicable fee. Claims 1-12 and 24-25 are currently pending and have been finally rejected. Applicants respectfully submit that the rejections of record are clearly not proper and request that the rejections be withdrawn.

The claims of the present application are directed to multi-particulate pharmaceutical dosage forms containing a population of extended release beads. The extended release beads include an active-containing core particle comprising cyclobenzaprine and/or pharmaceutically acceptable salts or derivatives of cyclobenzaprine and an extended release coating comprising a water insoluble polymer membrane surrounding the core. The claimed dosage form exhibits a drug release profile substantially corresponding to the following pattern:

after two hours, no more than about 40% of the active is released;

after four hours, from about 40%-65% of the total active is released; and

after eight hours, from about 60%-85% of the total active is released.

Furthermore, the dosage form provides therapeutically effective plasma concentration of the active over a period of twenty-four hours to treat muscle spasm associated with painful musculo-skeletal conditions when administered to a patient in need thereof. Dependent claims are also directed to various pharmacokinetic properties of the dosage form.

Claims 1-11 and 24-25 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Patel et al. U.S. 2003/0215496. Patel et al. broadly disclose solid pharmaceutical compositions comprising a solid carrier. A solid carrier may be composed of a substrate and an encapsulation coat, wherein the encapsulation coat contains combinations of active ingredients, hydrophilic surfactants, lipophilic surfactants and triglycerides or the solid carrier itself may be formed from a combination of active ingredients, lipophilic surfactants, hydrophilic surfactants and triglycerides. The document recites a lengthy list of active ingredients that can be included in the compositions and provides sweeping reference to an exhaustive list of preparation techniques, coatings and release profiles. The clear teachings of Patel to one of ordinary skill in the art relate to incorporation of solubilizing amounts of a hydrophilic surfactant to improve dissolution rate profiles for a pharmaceutical active ingredient present in a pharmaceutical composition in the form of a solid carrier. The document fails to provide any teaching or suggestion that would lead one of ordinary skill in the art to the composition set forth in the claims of the pending application.

Anticipation requires that the cited document "describe the applicant's claimed invention sufficiently to have placed a person of ordinary skill in the field of the invention in possession of it." *In re Spada,* 911 F.2d 705, 708, 15 U.S.P.Q. 2d 1655, 1657 (Fed. Cir. 1990). Furthermore, anticipation requires each and every element of the claim must be disclosed in the cited reference and "enable one skilled in the art to make the anticipating subject matter." *PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1566, 37 U.S.P.Q. 2d 1618, 1624 (Fed. Cir. 1996).

Initially, applicants note that Patel et al. fails to disclose or suggest the drug release profile set forth in the claims of the pending application and, furthermore, fails to disclose the functional limitation in claim 1 referring to the dosage form providing therapeutically effective plasma concentration over a period of twenty-four hours. These claim limitations, although functional, must be considered as any other limitation in the claims and this limitation has clearly not been shown as being disclosed in the Patel reference.

Furthermore, Patel fails to disclose applicant's claimed invention in such a way so as to place one of ordinary skill in the art in possession of the invention. Although Patel et al. disclose cyclobenzaprine in a laundry list of actives, and refers to essentially every type of release profile that is known to one of ordinary skill in the art, this falls far short of providing sufficient direction to one of ordinary skill in the art to make the claimed dosage form. One of ordinary skill in the art reading the Patel et al. reference would never be led to pick and choose the various components in just the right combination to provide a multi-particulate pharmaceutical dosage form characterized by a modified release profile that contains a population of extended release beads having the profile set forth in the claims of the pending application. Therefore, applicants respectfully submit that the rejection of claims 1-11 and 24-25 over Patel et al. is improper and should be withdrawn.

Claims 1-4, 6-11 and 24-25 stand rejected as being anticipated by Meadows et al. U.S. 2003/0099711. Meadows fails to anticipate for the same reasons as set forth above with respect to the Patel reference. Meadows relates to oral pharmaceutical preparations that contain a pharmacologically active drug bound to small particles of an ion exchange resin. The drug-resin complexes are coated with an aqueous based diffusion barrier comprising a water-permeable, film forming polymer that is relatively insoluble in gastro-intestinal fluids to provide sustained release the drug. Again, the only reference to cyclobenzaprine is in a list of drugs nearly two columns long. One of ordinary skill in the art appreciates the fact that formulating pharmaceutical compositions is an unpredictable art and teachings with respect to certain active ingredients are not necessarily applicable to other actives. Cyclobenzaprine is not set forth in any of the examples and there is no assurance that cyclobenzaprine would form a releasably bound complex with an ion exchange resin as set forth in the Meadows et al. document. Furthermore, there is no indication or suggestion in the cited document that would lead one to a

multi-particulate pharmaceutical dosage form as set forth in the claims of the pending application having the specified release profile. The disclosure in the Meadows document would fail to lead one of ordinary skill in the art how to make the claimed invention without undue experimentation. In response to applicant's previous arguments, the Examiner indicated that "under absence of showing unexpected results, the claims of Meadows render the same composition as applicant's instant claims, and the release profiles would be [sic] therefore be similar." June 13, 2007, Office Action, page 7. However, this statement fails to take into account the fact that the claims of Meadows fail to render this same composition as applicant's claims as there are significant differences between the two. The broad disclosure in Meadows fails to provide any suggestion at all that the dosage forms would have the same release profile set forth in the claims of the pending application. Accordingly, applicants respectfully submit that the claims of the present application are novel and non-obvious over the prior art of record and submit that the rejection is improper.

In view of the foregoing, it is respectfully submitted that the rejections of record are clearly not proper and that the claims currently pending are distinguishable from the references cited and in condition for allowance. Applicants respectfully request that a Notice of Allowability be issued in this case. Any questions concerning this application may be directed to applicant's undersigned attorney at the telephone number indicated below.

Respectfully submitted,

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